PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA2004/000648	30.04.2004	30.04.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/595, C07K14/50, A61K38/33, A61K38/18, C12N15/09, A01K67/027, A61P3/10

Applicant
WARATAH PHARMACEUTICALS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Fayos, C

Telephone No. +49 89 2399-2180

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-68 completely; claims 23-28, 31-36, 40-62 industrial applicability in particular

because:

☒ the said international application, or the said claims Nos. claims 23-28, 31-36, 40-62 industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-68 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☒ the claims, or said claims Nos. 1-68 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	-
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	23-28, 31-36, 40-62 see separate sheet
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1- Claims 23-28, 31-36, 40-62 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2- Although claims 1, 23, 24, 29, 30, 31, 32, 33, 34, 35, 36, 37, 40, 41, 42, 44, 56, 59, 60, 63, 67, 68 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

2.1- Therefore, no opinion is to be formulated on the novelty and inventive step for the subject matter of claims 1-68.

3- Furthermore, claims 1-20, 23-68 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved or in an unclear manner (KGF **agonist**, gastrin **compound**, gastrin/CCK **receptor ligand**) which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

3.1- In addition, claims 1-68 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description. The description only provides support in terms of technical data for the combination KGF/gastrin (see examples).

If the applicant does not restrict the subject matter of claims 1-68 to the combination KGF/gastrin (Art. 6 PCT), then he should indicate why it is believed that the other claimed, but non-exemplified possibilities are active. It should be borne in mind that a technical effect solving a technical problem has to be achieved by all embodiments falling within the scope of the claim.

4.2- Furthermore, since the present application provides **one single example** of combination (namely gastrin / KGF), claims 1-68 lack clarity, support and disclosure (Arts. 6 and 5 PCT), since the skilled person, after reading the description, would not able to perform the invention over the whole area claimed without undue burden and without needing inventive skill.

Indeed, the claims encompass a genus of compounds defined only by their function wherein the relationship between the structural features of the members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the application as originally filed or which would have been recognised based on information readily available to the skilled man, the skilled person would not know how to make and use compounds that lack any structural definition. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity.

4.3- Hence, no opinion with regards to the novelty, inventive step and industrial applicability is to be formulated for the subject matter of present claims 1-68.

For the sake of completeness, the following is to be noted:

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

5- The following documents are cited; the relevant passages are those indicated in the search report, unless otherwise specified:

D1: US-A-5 858 977 (AUKERMAN SHARON LEA ET AL) 12 January 1999 (1999-01-12)

D2: WO 00/44400 A (RTP PHARMA INC ; GEN HOSPITAL CORP (US)) 3 August 2000 (2000-08-03)

D3: YAMAOKA T ET AL: "Development of pancreatic islets (review)." INTERNATIONAL JOURNAL OF MOLECULAR MEDICINE. MAR 1999, vol. 3, no. 3, March 1999 (1999-03), pages 247-261, XP009037276 ISSN: 1107-3756

D4: LOGSDON CRAIG D ET AL: "Adenoviral-mediated gene transfer of dominant negative ras inhibits pancreatic acinar cell growth responses to cholecystokinin and fibroblast growth factor" GASTROENTEROLOGY, vol. 112, no. 4 SUPPL., 1997, page A458, XP009037266 & DIGESTIVE DISEASE WEEK AND THE 97TH ANNUAL

MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION; WASHINGTON, D.C., USA; MAY 11-14, 1997 ISSN: 0016-5085

5.1- As mentioned above, no opinion will be formulated with regards to the novelty and inventive step for the subject matter of claims 1-68. It should be noted however, that the combination of KGF and gastrin for the treatment of diabetes and related diseases appears obvious from D1, taken in combination with D2.

6- For the assessment of the present claims 23-28, 31-36, 40-62 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

7- When / if carrying out amendments, and in order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter wether they concern amendments by addition, replacement or deletion, and to indicate precisely the passages of the application as filed on which these amendments are based (also rule 66.8 (a) PCT).

Only amendments with a clearly identified basis on the application as originally filed will be taken into account for the international preliminary examination report.